Addiction

CASE REPORT

doi:10.1111/j.1360-0443.2008.02209.x

Self-treatment of opioid withdrawal using kratom (*Mitragynia speciosa korth*)

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ABSTRACT

Background Kratom (*Mitragynia speciosa korth*) is recognized increasingly as a remedy for opioid withdrawal by individuals who self-treat chronic pain. **Case description** A patient who had abruptly ceased injection hydromorphone abuse self-managed opioid withdrawal and chronic pain using kratom. After co-administering the herb with modafinil he experienced a tonic-clonic seizure, but he reported only modest abstinence once kratom administration stopped. We confirmed the identity of the plant matter he ingested as kratom and identified no contaminants or adulterants. We also conducted high-throughput molecular screening and the binding affinity at mu, delta and kappa receptors of mitragynine. **Conclusion** We report the self-treatment of chronic pain and opioid withdrawal with kratom. The predominant alkaloid of kratom, mitragynine, binds mu- and kappa-opioid receptors, but has additional receptor affinities that might augment its effectiveness at mitigating opioid withdrawal. The natural history of kratom use, including its clinical pharmacology and toxicology, are poorly understood.

Keywords Dependence, kratom, molecular screening, opioid, opioid replacement, withdrawal.

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Submitted 23 November 2007; initial review completed 17 January 2008; final version accepted 8 February 2008

INTRODUCTION

Kratom (*Mitragynia speciosa korth*) is a medicinal herb indigenous to Southeast Asia whose components mitragynine and 7-hydroxymitragynine agonize the mu-opioid receptor with high affinity [1–3]. Recent findings suggest that kratom is purchased from internet sources by some of the 40 million Americans with chronic pain to self-manage opioid withdrawal [1]. Unfortunately, the reasons underlying this practice, its efficacy or adverse effects are poorly understood. We present a case of kratom used to self-manage chronic pain and opioid withdrawal complicated by a potential interaction with modafinil.

CASE PRESENTATION

A 43-year-old male was admitted for evaluation of a generalized tonic-clonic seizure. His medical history included chronic pain from thoracic outlet syndrome treated with hydromorphone. As his tolerance escalated, he began injecting subcutaneously 10 mg hydromorphone per day from crushed pills. During periods when hydromorphone was unavailable, he managed opioid withdrawal with kratom purchased from internet vendors.

Approximately 3.5 years before presentation, social stressors compelled him to quit hydromorphone abruptly. He again averted opioid withdrawal by ingesting a tea made from kratom four times a day. The patient attributed substantial pain relief to kratom as well as improved alertness. He did not, however, experience the drowsiness that often accompanied opioid use. He spent $15 000 per year on kratom, a sum confirmed by his wife.

In an attempt to improve alertness further, the patient experimented with the co-administration of 100 mg modafinil with kratom. Twenty minutes following ingestion, he experienced a generalized tonic-clonic seizure lasting 5 minutes. He had the following vital signs on

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presentation: pulse 123 beats per minute, blood pressure 130/74 mm/Hg, respiratory rate 16; he was afebrile. After a brief post-ictal period, his physical examination was normal except for meiosis. He had no previous history of seizures or head trauma, and he denied alcohol or recent illicit drug abuse. Laboratory studies were unremarkable; qualitative urine drugs of abuse and comprehensive toxicology screening identified only modafinil. Computerized tomography and magnetic resonance imaging of the brain were normal. We identified no adulterants or contaminants. Upon discharge, the patient abruptly ceased use of kratom and sought the care of an addiction specialist.

He described a period of withdrawal considerably less intense but more protracted than that from prescription opioids. Physician-observed features of kratom included rhinorrhea, insomnia, poor concentration, constricted affect and myalgias persisting for 10 days from his last dose of kratom. To prevent relapse, an addiction specialist prescribed buprenorphine/naloxone, reaching a maintenance dose of 16 mg per day. Rhinorrhea ceased on the first day of suboxone therapy. The patient currently reports adequate pain control, and follow-up urine screens for drugs of abuse have remained negative. We confirmed the identity of the plant matter ingested by the patient as kratom by comparison against a known standard (Pure Land Ethnobotanicals, Madison, WI, USA) utilizing existing extraction and high-performance liquid chromatography protocols.

DISCUSSION

We report the protracted use of kratom for chronic pain treatment and opioid replacement therapy. Opioid analgesics remain highly effective modalities for the treatment of chronic pain, but their long-term administration is associated with the development of opioid misuse, abuse, dependence and addiction, the incidence of which is increasing [4]. Among individuals with chronic pain who are maintained on opioid analgesic agents, kratom is gaining awareness as a 'natural' alternative to physician-supervised opioid replacement therapy [1].

One striking finding of this report is the extent to which kratom attenuates potentially severe opioid withdrawal, yet cessation of kratom administration itself appears to be associated with modest abstinence symptoms. The pharmacological bases underlying this effect are uncertain. For example, mitragynine is theorized to stimulate contributions from adrenergic and serotonergic pathways that augment analgesia, but formal binding data have been obtained only for mu-, delta- and kappa-opioid receptors [5,6]. To delineate more clearly the *in vitro* pharmacology of kratom, we conducted high-throughput molecular screening of mitragynine activity at central nervous system receptors (Novascreen Biosciences Corp., Hanover, MD, USA); these studies identified that mitragynine extensively inhibits radioligand binding at several central nervous system receptor systems (Table 1). The clinical implication of these results is that mu-opioid agonism may avert withdrawal symptoms, while kappa agonism attenuates reinforcement and produces aversion [7]. In addition, mitragynine, through its putative alpha-2 adrenergic agonist activity, may mimic adjunctive therapies for opioid withdrawal such as clonidine. Mitragynine, therefore, may exert several convergent pharmacological effects that could attenuate opioid withdrawal symptoms and blunt cravings.

Table 1 Central nervous system receptor binding data for mitragynine.

Percentage inhibition of radioligand binding by mitragynine at selected receptor systems
Adenosine A2A: 65.66
Adrenergic (Alpha 2): 61.92
Dopamine D2s 54.22
Opioid, mu 89.52
Opioid, kappa 90.21
Opioid, delta 7.00
Serotonin, 5HT2C 58.77
Serotonin, 5HT7 64.41
Dissociation constants for opioid receptor binding
Mu receptor: 204 ± 26 nM
Delta receptor: 2250 ± 120 nM
Kappa receptor: 455 ± 47 nM

Adverse effects from kratom are poorly described. Although mitragynines agonize mu-opioid receptors, respiratory depression, coma, pulmonary edema and death have not, to our knowledge, been associated with human kratom ingestion. Furthermore, the protracted use of kratom as a single therapy did not appear to produce any significant adverse effects in this patient; not until co-administration with modafinil was a potential adverse effect of kratom identified. The exact mechanisms that contribute to seizure are undefined. The mitragynines, their metabolites or other components of kratom could potentially exhibit proconvulsant properties similar to atypical opioids such as tramadol, the meperidine metabolite normeperidine and propoxyphene [8]. Synergism between kratom and modafinil might also produce seizure, but considering that modafinil is not likely to possess proconvulsant properties, this latter mechanism appears speculative.

The risk correlates of kratom use as well as outcomes from its long-term administration are unknown. Initiation of kratom use may reflect increasing interest in alternative therapies for chronic medical problems [9,10]. Alternatively, some patients with chronic pain may per-

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ceive that formal drug treatment is reserved for users of illegal substances [1]. Finally, patients' satisfaction with existing systems that treat chronic pain or problematic opioid use—which frequently underprescribe analgesics, require treatment contracts, demand ongoing drug testing or stigmatize those who seek care—may be so poor that some patients shun physician contact [1,11]. In this last population, whether self-treatment with kratom can avert problematic opioid analgesic use is uncertain. Further research into the natural history of kratom ingestion, its neuropsychiatric effects, as well as its clinical pharmacology and toxicology, will place the risks and benefits of kratom administration into clearer perspective.

Acknowledgment

Funding for this study was provided in part by NIDA grants DA022677 and DA014929 (P. I, Boyer); also by National Center for Research Resources grant P20RR021929 (C. R. McCurdy). Patient consent was obtained.

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